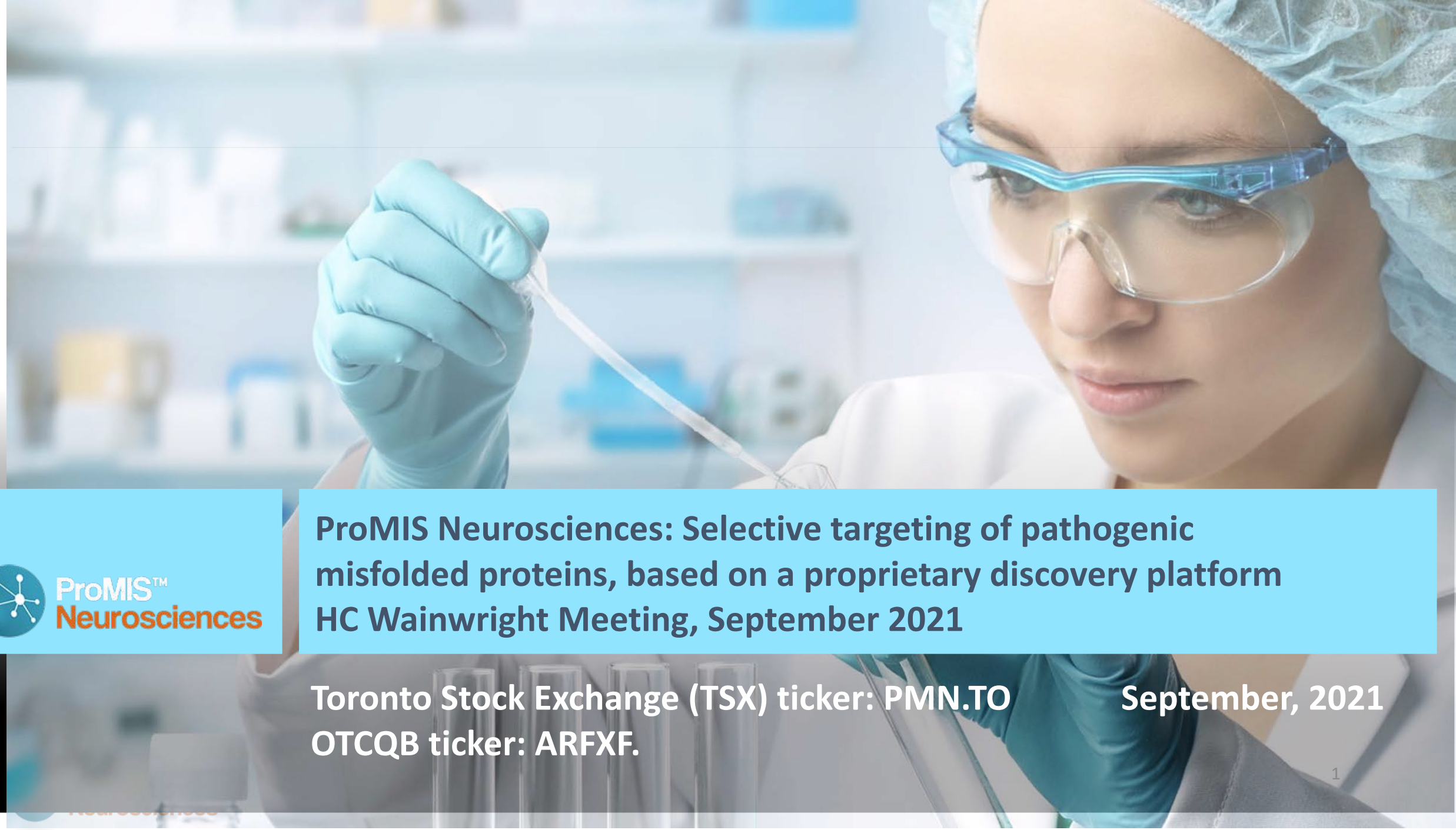


ProMIS Neurosciences: Selective targeting of pathogenic misfolded proteins, based on a proprietary discovery platform
HC Wainwright Meeting, September 2021

Toronto Stock Exchange (TSX) ticker: PMN.TO
OTCQB ticker: ARFXF.

September, 2021

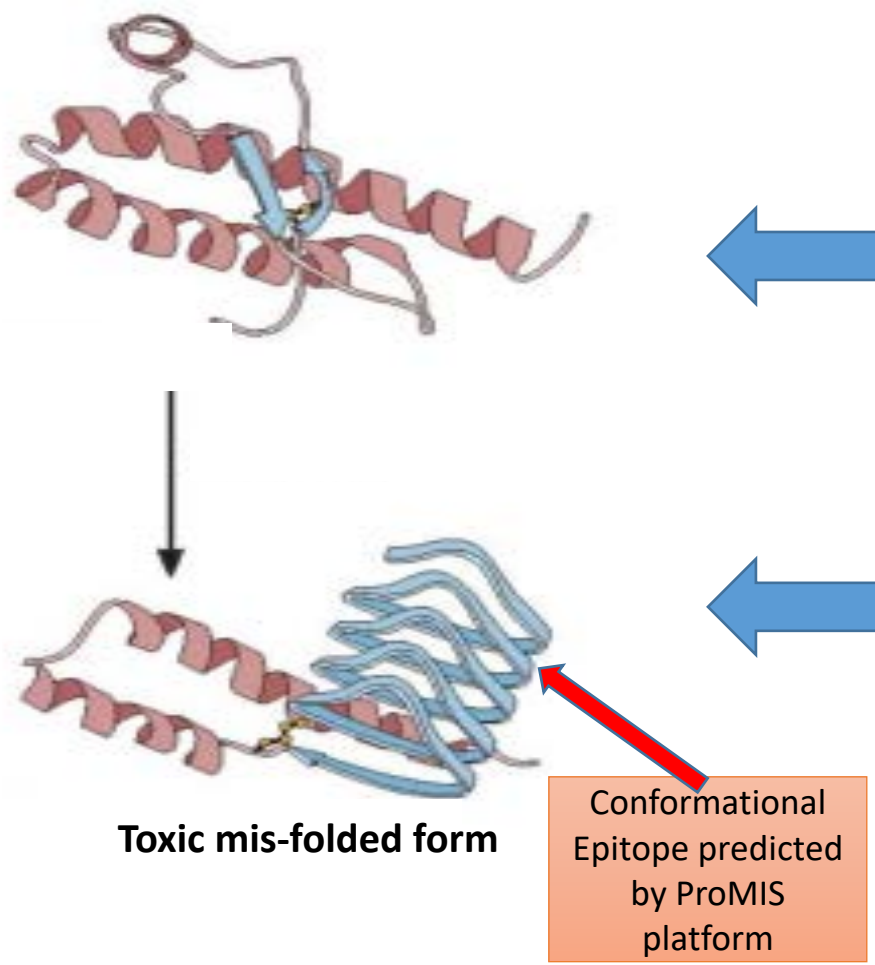
Forward looking statement: safe harbor

This slide deck may contain certain forward-looking information. Such information involves known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements to be materially different from those implied by statements herein, and therefore these statements should not be read as guarantees of future performance or results. All forward-looking statements are based on the Company's current beliefs as well as assumptions made by and information currently available to it as well as other factors. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this slide deck. Due to risks and uncertainties, including the risks and uncertainties identified by the Company in its public securities filings available online at www.sedar.com. Actual events may differ materially from current expectations. The Company disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

ProMIS Summary

- Differentiated ***technology platform*** – Computational approaches to rational design of selective antibodies for mis-folded proteins implicated in disease, a unique ProMIS capability
- High selectivity a ***ProMIS competitive advantage.*** Lack of selectivity for mis-folded proteins likely the primary source of failures or limited success in prior competitor programs in neurodegenerative diseases
- ***Lead program PMN310 potential "best of the next generation" antibody therapy in Alzheimer's disease:*** highly selective for toxic oligomer form of amyloid, differentiated from likely first generation products from Biogen, Eisai, and Lilly; PMN310 differentiated from first oligomer selective antibody from Acumen
- Fluid-based biomarkers may enable ***rapid and capital efficient path to clinical readout*** and value inflection for all programs
- ***Growing portfolio*** of antibodies ***selective for mis-folded proteins*** implicated in neurodegenerative diseases
- Recently completed $20.125 MM financing, fully funded through 2022, to IND filing for lead program

Mis-folded proteins have the same amino acid sequence as normal proteins…the only difference is the shape…ProMIS identifies conformational epitopes exposed only on mis-folded proteins



Normal protein – folds into a specific shape to perform its physiologic function

Mis-folded protein…improper folding exposes toxic portions of the protein…..in a particular shape or conformation…

ProMIS platform predicts conformational epitopes – both amino acid sequence and shape, only exposed on toxic mis-folded proteins….

Immunizations with those epitopes lead to selective antibodies

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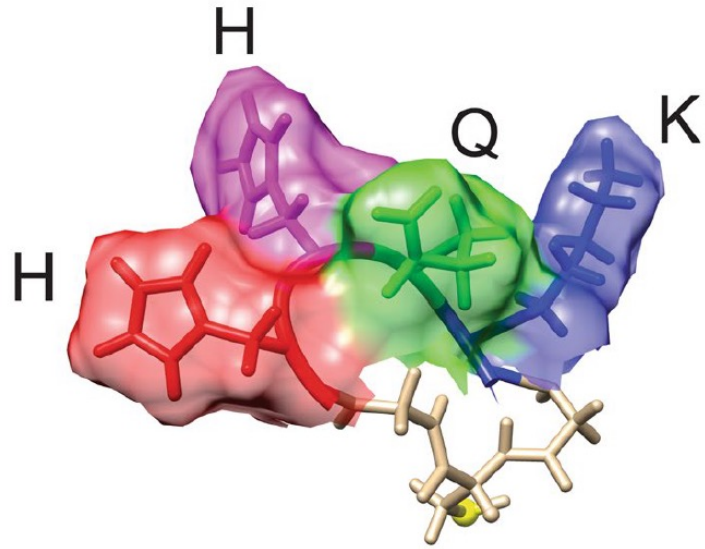
Image adapted from Racaniello V et al, virology.ws, 2016

PMN310: an anti-Aβ-oligomer antibody with strong potential to demonstrate best-in-class characteristics in Alzheimer's treatment

- ***ProMIS at AAIC 2021 – breakthrough scientific finding***

- "*Conformational epitopes exposed on misfolded toxic forms of amyloid-beta, tau and alpha-synuclein directly contribute to their seeding activity"*

- Exposed epitopes play a direct role in disease progression



Aβ amino acids 13-16 (HHQK) form a unique, Aβ oligomer specific conformational epitope targeted by PMN310

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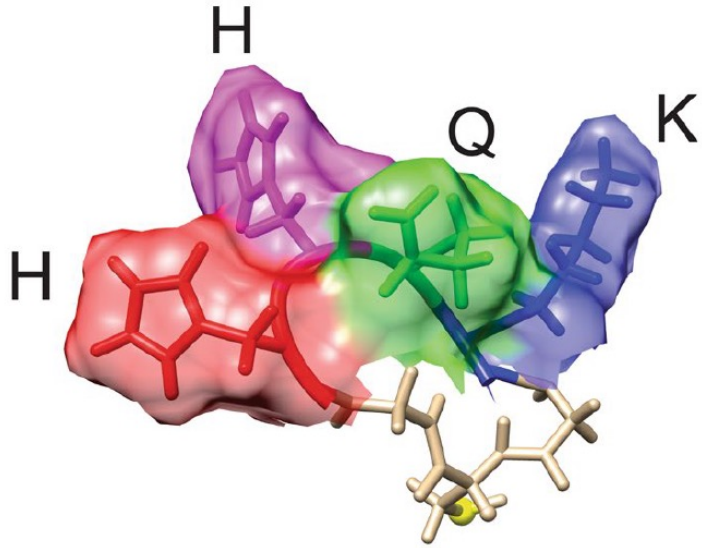
PMN310: an anti-Aβ-oligomer antibody with strong potential to demonstrate best-in-class characteristics in Alzheimer's treatment

PMN310 is a next-generation, best-in-class anti-amyloid therapy

- **Highly selective for <u>only</u> toxic oligomers**
  - Does not bind monomer
  - Does not bind plaque → ***likely no ARIA-E side effect***

- Dose expected not to be limited by off-target binding or side effects
- All dosed PMN310 will be focused on neutralizing toxic oligomers

  → ***potentially greater clinical efficacy***



Aβ amino acids 13-16 (HHQK) form a unique, Aβ oligomer specific conformational epitope targeted by PMN310

First generation therapies Aducanumab (Biogen), BAN2401 (Eisai), donanemab (Lilly) bind <u>all</u> aggregated amyloid – plaque and oligomers

- Modest efficacy validates mechanism
- All bind amyloid plaque leading to poor safety profile → ARIA-E (brain swelling)
- None bind monomer (the physiologic amyloid species)

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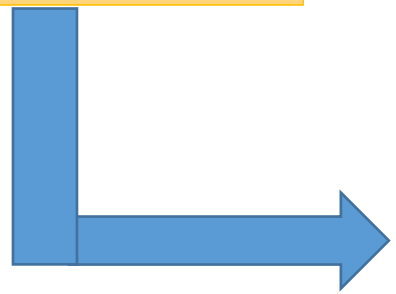
Degree of selectivity for the correct (toxic) form of amyloid explains past clinical results

Forms of Amyloid

Monomer – Important for brain health

Mis-folded Toxic oligomers – thousands of scientific studies showing neurotoxicity

Plaque – usually present, but no significant role in disease



Aggregated amyloid

Builds up when production of amyloid exceeds clearance

ProMIS™ Neurosciences

Degree of selectivity for the correct (toxic) form of amyloid explains past clinical results

Forms of Amyloid	**Monomer** – Important for brain health	**Mis-folded Toxic oligomers** – thousands of scientific studies showing neurotoxicity	**Plaque** – usually present, but no significant role in disease

"it is commonly thought that Ab ***oligomers***, not monomer, or plaques, may be the primary toxic species"

Biogen publication in Nature, Sep 1 2016

Aducanumab….directly inhibits the molecular process through which oligomers form (secondary nucleation), thereby reducing the formation of ***neurotoxic Ab oligomers…"***

FDA Advisory Committee Briefing document for Biogen's Aducanumab November 2020

Degree of selectivity for the correct (toxic) form of amyloid explains past clinical results

Forms of Amyloid	**Monomer** – Important for brain health	**Mis-folded Toxic oligomers** – thousands of scientific studies showing neurotoxicity	**Plaque** – usually present, but no significant role in disease
Amyloid Binding profile of clinical programs	**10** programs/**25** phase 2 and 3 clinical trials **targeting monomer** **All negative – 0/25**		
	4 programs/**13** phase 2 and 3 clinical trials **non-selectively targeting all forms of amyloid** **All negative – 0 / 13**		
		Three drugs: Biogen's aducanumab approved, EISAI's BAN2401, Lilly's donanemab positive phase 2– selective for *aggregated amyloid* **ALL POSITIVE**	
		PMN310 **potential best in class**, selective for toxic oligomers	

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There are three forms of amyloid, PMN310 is differentiated by selective binding of the toxic form (oligomers)

Bapineuzumab (Pfizer)
- Phase 2 failure
- Phase 3 failure
- ARIA-E side effect

Solanezumab (Eli Lilly)
- Phase 2 failure
- Phase 3 failure

Aducanumab (Biogen)
- Phase 2 & 3 success
- ARIA-E side effect

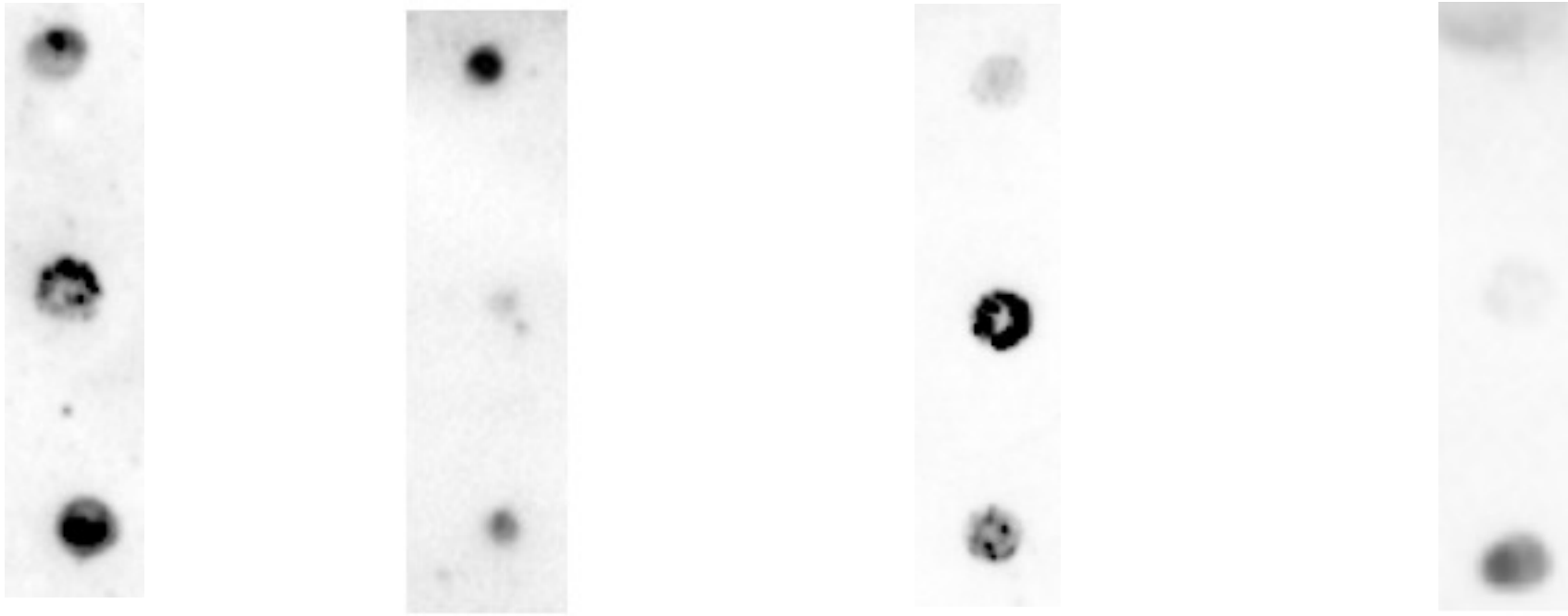
PMN310
- Selective binding to oligomers

-> Expected improvement in efficacy & safety

MONOMERS
- binding wastes therapeutic ammunition

FIBRILS (Plaque)
- binding wastes therapeutic ammunition
- contributes to ARIA-E side effect

OLIGOMERS*
- the right target



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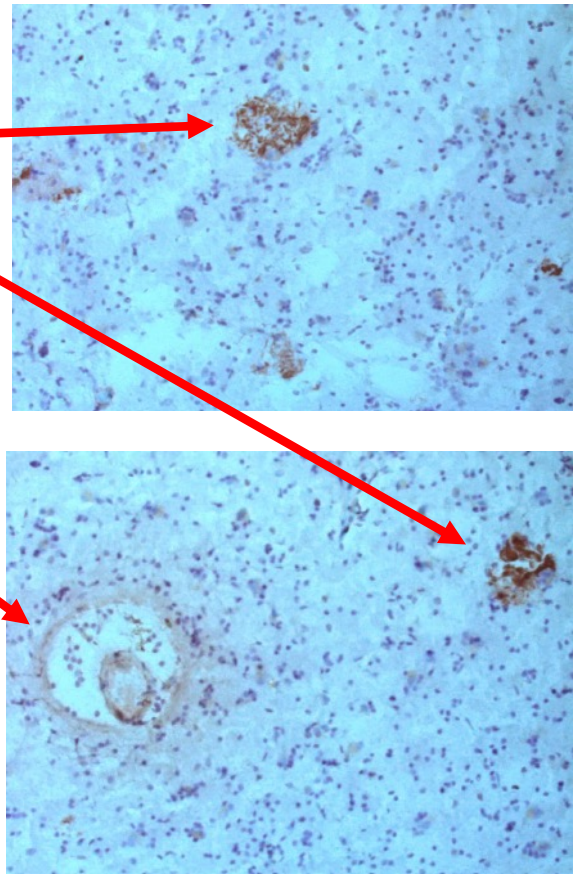
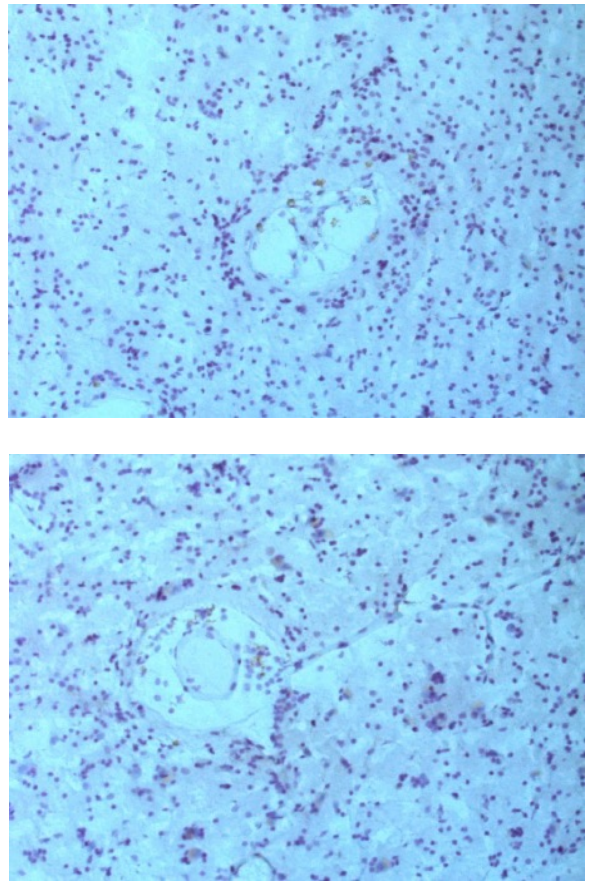
* Synthetic oligomers

ARIA-E associated with aducanumab, BAN2401 & bapineuzumab; PMN310 lack of binding to Aβ plaque strongly suggests a *potential safety advantage - no ARIA-E*

Aducanumab



PMN310



No binding to plaque or vascular deposits

Most likely no ARIA-E*

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* ARIA-E (Amyloid Related Imaging Abnormality-Edema) also known as brain swelling

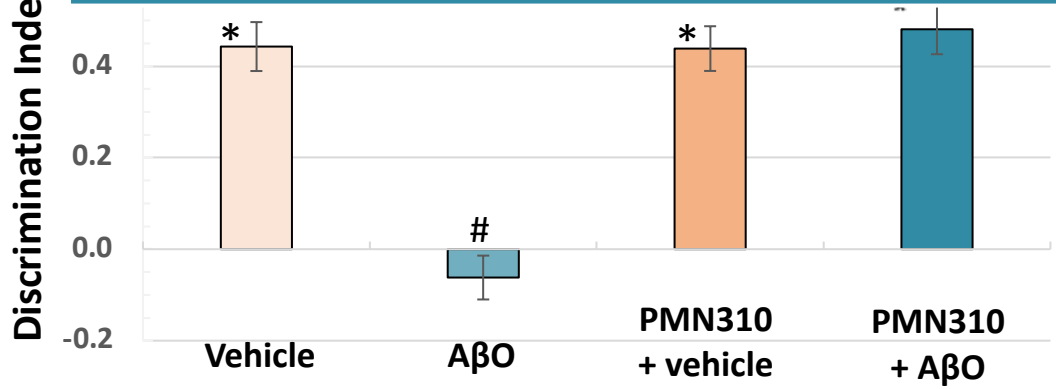
Administration of PMN310 to mice prevents loss of short-term memory formation caused by toxic oligomers, by saving mouse neurons

THE EXPERIMENT

- Mice are tested for discriminating objects after brain injection of:
  - Buffer (vehicle) - normal response
  - Toxic Aβ oligomer
  - PMN310 and buffer (vehicle)
  - PMN310 and Aβ Oligomer

7 days

THE RESULTS



N=12 per arm, *different from AβO ($p < 0.05$), #different from vehicle ($p < 0.05$)

Novel Object Recognition Assay

- **Control mice remember a familiar object when re-exposed to it and spend more time exploring a new object**
- **Oligomer-injected mice lose the ability to discriminate between known and novel objects and spend equivalent amounts of time exploring both**

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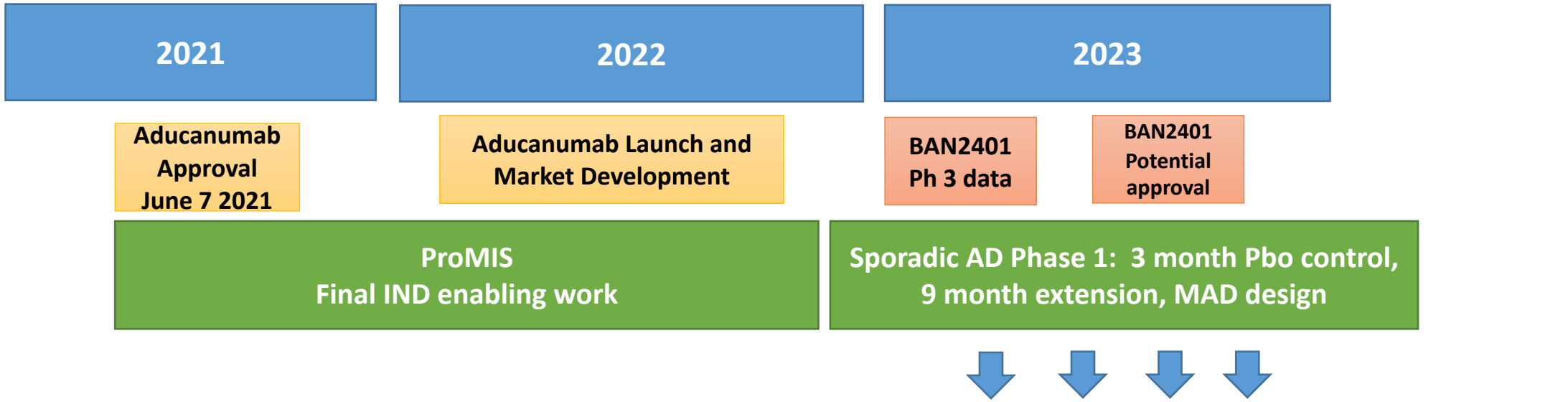
Discrimination index = (Time exploring new object – time exploring familiar object) / total exploration time
Results press released January 9, 2017, www.promisneurosciences.com

PMN310: potential for value-creating clinical data in the near term

- likely positive market developments could amplify PMN value



Open label after 3 months of treatment
Ongoing biomarker readouts could provide signal

- Recent advances in blood-based biomarkers may allow ProMIS to detect an objective treatment signal as early as Phase 1, potentially providing rapid & cost-effective proof-of-concept

PMN310:
potentially "best of the next generation" therapy in Alzheimer's

Amyloid beta-targeted therapies

All BACE inhibitors

Non-selective antibodies

Monomer-targeted antibodies

Aduhelm (Biogen, Approved)

BAN2401 (Eisai, Positive Ph2)

Donanemab (Lilly, Positive Ph2)

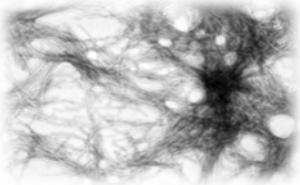
ACU193 (Acumen, Ph1 start June 2021
Recent NASDAQ IPO)

PMN310 – best in class:

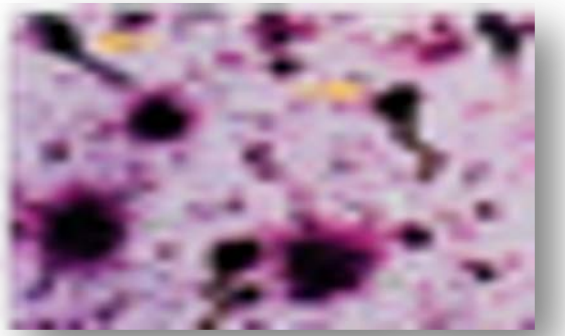
- ***High selectivity for toxic oligomers***
- ***Effector Function (IgG1)***
- ***Potential subcutaneous delivery***

Alzheimer's, Parkinson's and ALS are protein misfolding diseases, where the toxic mis-folded proteins propagate in a prion-like manner

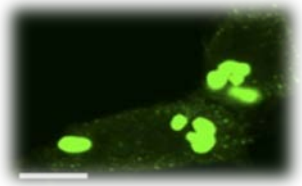
Huntington's disease
(huntingtin)



Alzheimer's disease
(amyloid-beta and tau)

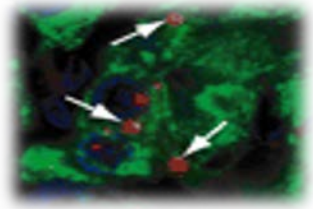


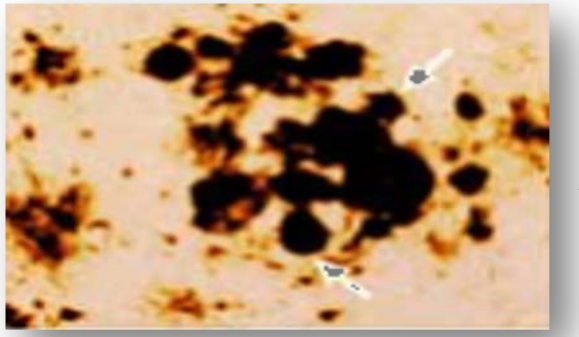
Schizophrenia
(DISC1)



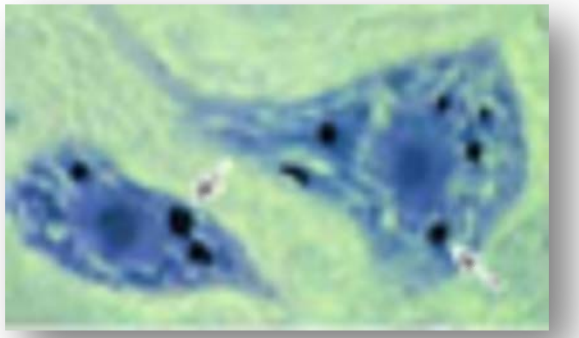
Senile amyloidosis
(transthyretin)

Type 2 diabetes
(amylin)

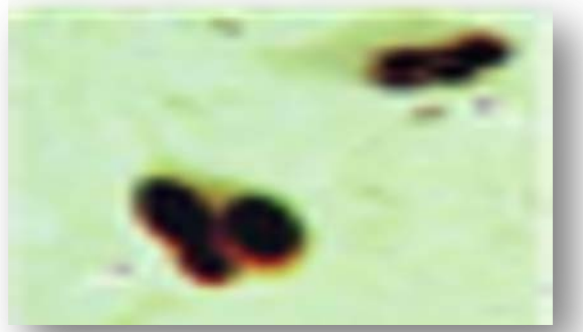




Prion diseases
(prion protein)



ALS
(TDP43, SOD1, FUS)



Parkinson-like diseases
(alpha-synuclein)

ProMIS: a broad differentiated portfolio; a unique technology platform

- *Potential "best of the next generation" for all of neurodegenerative disease*

Misfolded protein target	Lead indication	Other Indications	Status
Amyloid beta	Alzheimer's		IND enabling work ongoing
TDP-43	ALS	FTD, LATE	Lead antibodies
Alpha synuclein	Multiple System Atrophy	Parkinson's, LBD	Lead antibodies
tau	Alzheimer's	PSP, other tauopathies	Lead selection
SOD1	ALS		Lead antibodies
RACK1	ALS	HD, cancers	Immunizations
Ataxin2	ALS		Computational modeling
Disc1	ALS	Schizophrenia	Computational modeling
Amylin	T2Diabetes		Computational modeling

DLB: Dementia with Lewy bodies, FTD: Frontotemporal dementia, LATE: Limbic-predominant age-related TDP-43 encephalopathy, ALS: Amyotrophic lateral sclerosis, PSP: Progressive supranuclear palsy, AD: Alzheimer's disease, HD: Huntington's disease

ProMIS: Potential near and medium term catalysts

- **Clinical/Regulatory**
  - Data from PMN310 formulation work further supporting potential for subcutaneous delivery
  - PMN310 program progress – GMP manufacturing start, GLP tox data
  - Further PMN310 in vivo data
  - Complete PMN310 IND enabling studies, prepare for clinical trial start 2H '22
- **Pipeline development**
  - In vivo and in vitro data from TDP-43, alpha synuclein, and other programs
  - IP filings and antibody candidates against novel mis-folded protein targets
- **Finance/Operational**
  - Evaluate possible NASDAQ listing
  - Strengthen Board and Management

ProMIS Summary

- Differentiated ***technology platform*** – Computational approaches to rational design of selective antibodies, a unique ProMIS capability
- ***Growing portfolio*** of antibodies ***selective for mis-folded proteins*** implicated in neurodegenerative diseases
- High selectivity a ***ProMIS competitive advantage.*** Lack of selectivity for mis-folded proteins likely the primary source of failures or limited success in prior competitor programs in neurodegenerative diseases
- ***Lead program PMN310 potential "best of the next generation" antibody therapy in Alzheimer's disease:*** highly selective for toxic oligomer form of amyloid, differentiated from likely first generation products from Biogen, Eisai, and Lilly; PMN310 differentiated from first oligomer selective antibody from Acumen
- Multiple programs 21-36 months from clinical data – IND enabling work followed by SAD/MAD trial in patients; Fluid-based biomarkers may enable ***rapid and capital efficient path to clinical readout*** and value inflection for all programs
- Recently completed $20.125 MM financing, fully funded through 2022, to IND filing for lead program

Thank You

Please feel free to contact us with any additional questions.

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https://www.linkedin.com/company/promis-neurosciences

ProMIS™ Neurosciences

Experienced leadership team

Name	Title	Years of Experience	Prior Experience
Gene Williams	Executive Chairman	25+	▪ Former SVP at Genzyme, with senior roles integrating commercialization, drug development, and deal making ▪ Recently the CEO of Dart Therapeutics, an Orphan Disease drug development company ▪ Founder and director of Adheris, which became the largest company in the patient adherence/compliance area
Elliot Goldstein	CEO	25+	▪ Held positions as SVP of Strategic Product Development at SmithKline Beecham (now GSK) ▪ Chief Operating Officer and Chief Medical Officer of Maxygen ▪ Chief Operating Officer at DART Therapeutics
Neil Cashman	Chief Science Officer	25+	▪ Holds the Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases, ▪ Serves as the Director of the University of British Columbia ALS Centre, ▪ Awarded the Jonas Salk Prize for biomedical research in 2000
David Wishart	Chief Physics Officer	25+	▪ Distinguished University Professor in the Departments of Biological Sciences and Computing Science at the University of Alberta ▪ Co-Director of The Metabolomics Innovation Centre ▪ Bristol-Myers Squibb Research Chair in Pharmaceutical Sciences 1995-2005 ▪ Fellow of the Royal Society of Canada
Dan Geffken	CFO	25+	▪ Founding Managing Director of Danforth Advisors ▪ Served as the Chief financial officer of Homology, Inc, GenePeeks, Inc., Transkaryotic Therapies, Inc., Cidara, Inc., Apellis, Inc. and Stealth BioTherapeutics, Inc.
Johanne Kaplan	Chief Development Officer	25+	▪ Former VP of Research at Genzyme ▪ Associate Immunopathologist at SmithKline Beecham where she established an Immunotoxicology program ▪ Her work has resulted in over 60 scientific publications and multiple patents

Scientific Advisory Board

Name	Years of Experience	Prior Experience	Affiliations
Sharon Cohen, MD	20+	▪ Medical Director & Principal Investigator of Toronto Memory Program ▪ FRCPC in neurology from Royal College of Physicians of Canada and a fellowship in Behavioural Neurology from the University of Toronto	Toronto Memory Program
Rudy Tanzi, PhD (Chairman)	20+	▪ Professor of Neurology at Harvard University, Vice Chair of Neurology, Director of Genetics & Aging Research Unit, Co-Director McCance Center for Brain Health at Mass General Hospital	Harvard University; Massachusetts General Hospital
Bill Mobley, MD, PhD	25+	▪ Dean for Neurosciences Initiatives, Distinguished Professor of Neurosciences, and Florence Riford Chair for Alzheimer Disease at the University of California, San Diego	UC San Diego School of Medicine
James Kupiec, MD	20+	▪ Former VP, Global Clinical Leader for Parkinson's disease, and Clinical Head of the Neuroscience Research Unit for Pfizer, Inc. ▪ Clinical focus on development of therapies for neurodegenerative disorders	Ciba; Pfizer; sanofi~synthelabo
C. Warren Olanow, MD	25+	▪ Previous Henry P & Georgette Goldschmidt Professor & Chairman, Department of Neurology at Mount Sinai School of Medicine, presently Professor Emeritus Department of Neurology & Department of Neuroscience, CEO of CLINTREX	MSSM; Mount Sinai School of Medicine
Andre Strydom, MD, PhD	25+	▪ Professor Institute of Psychiatry, Psychology and Neuroscience at King's College London ▪ Honorary Consultant psychiatrist, South London and the Maudsley NHS Foundation Trust	King's College London; NHS South London and Maudsley NHS Foundation Trust
Michelle Hastings, PhD	20+	▪ Professor and Director, Center for Genetic Diseases, Rosalind Franklin University of Medicine and Science ▪ Faculty Member at the Chicago Medical School	Rosalind Franklin University of Medicine and Science